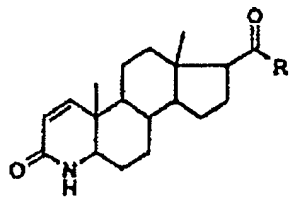
PROCESS FOR INTRODUCING A 1,2-DOUBLE BOND IN 3-OXO-4-AZASTEROID COMPOUNDS

ABSTRACT

[0048] A process for preparing 17β-substituted 4-azaandrost-1-en-3-one compounds of the general formula (I):



(I)

or a pharmaceutically approved salt thereof,

where

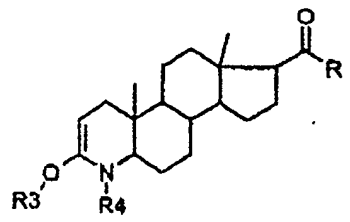
R is hydroxyl, optionally substituted, linear or branched (C_1-C_{12})alkyl or (C_1-C_{12})alkenyl; phenyl or benzyl; an -OR_1 radical, or an -NHR_1 radical, or an -NR_1R_2 radical;

R_1 is hydrogen, optionally substituted, linear or branched (C_1-C_{12})alkyl or (C_1-C_{12})alkenyl, or optionally substituted phenyl;

R_2 is hydrogen, methyl, ethyl or propyl; or

-NR_1R_2 is a 5- or 6-membered heterocyclic ring,

by (A) introducing protecting groups into the 3-keto-4-aza moiety of the corresponding 1,2-dihydro compound, so that a compound of the general formula (III) is formed:



(III)

where

R_3 is trialkylsilyl or, together with R_4, the -C(O)-C(O)- or -C(O)-Y-C(O)- radical;

R_4 is alkyloxycarbonyl or phenyloxycarbonyl, preferably Boc (= tert-butyloxycarbonyl); or trialkylsilyl, or, together with R_3, the -C(O)-C(O)- or -C(O)-Y-C(O)- radical;

Y is $-[C(R_5)(R_6)]_n-$ or $-CH(R_5)=CH(R_6)-$, or ortho-phenylene;

R_5 and R_6 are each independently hydrogen, linear or branched (C_{1-8})alkyl or alkenyl, optionally substituted phenyl or benzyl; and

n is an integer of 1 to 4;

and where, in the case that R is hydroxyl, it has optionally reacted with a protecting group;

(B) reacting the resulting compound in the presence (i) of a dehydrogenation catalyst, and in the presence of (ii) optionally substituted benzoquinone, allyl methyl carbonate, allyl ethyl carbonate and/or allyl propyl carbonate, and

(C) removing the protecting groups R_3 and R_4 and optionally converting the resulting compound to a salt.